Can the incidence of coronary heart disease be decreased by the use of a diet in which total fats are composed of approximately equal proportions of saturated, monounsaturated, and polyunsaturated fatty acids? The Anti-Coronary Club Project in New York now reports data indicating a favorable answer to this question. The conditions of the study are evaluated and its possibilities for further program action examined.

THE ANTI-CORONARY CLUB

A DIETARY APPROACH TO THE PREVENTION OF CORONARY HEART DISEASE—A SEVEN-YEAR REPORT

G. Christakis, M.D., F.A.P.H.A.; S. H. Rinzler, M.D.; M. Archer, M.S.; G. Winslow, M.D.; S. Jampel, M.D.; J. Stephenson, M.D.; G. Friedman, M.D.; H. Fein, M.D.; A. Kraus, Sc.D.; and G. James, M.D., F.A.P.H.A.

THE Anti-Coronary Club Study Project represents an epidemiological approach to a test of the hypothesis that adherence to a serum cholesterol-lowering diet will be associated with a decreased incidence of coronary heart disease.

The Diet and Coronary Heart Disease Study conducted by the Bureau of Nutrition of the New York City Department of Health has been in progress since 1957. In previous reports the composition of the experimental diet (or "Prudent Diet") has been described, and data presented which suggested that adherence to this diet can significantly lower the level of serum cholesterol of both normal and overweight coronary and noncoronary subjects.[1-13]

Concurrent with the maintenance of lowered level of serum cholesterol over a five-year period, a progressive increase in the per cent composition of linoleic acid in the depot fat of Anti-Coronary Club subjects has been observed.[14] According to present knowledge, linoleic acid, an essential unsaturated fatty acid, can only be derived from dietary sources. This observed increase in depot fat linoleic acid therefore indicates that adherence to the study diet has been satisfactory. Experimental demonstration of the serum cholesterol-lowering effect of diets relatively rich in polyunsaturated fats,[15-18] supports the conviction that our study diet is responsible for the long-term depression of serum cholesterol observed in Anti-Coronary Club subjects.

Recent investigations on the effect of the experimental diet on serum vitamin E and vitamin A levels of study subjects have affirmed the nutritional adequacy of the diet with respect to these nutrients.[19] Furthermore it was found that long-term adherence to the study diet has no demonstrable effect in increasing serum triglyceride levels. Finally, preliminary data have been published indicating that our Anti-Coronary Club experience may be associated with a decrease in coronary heart disease incidence based on a comparison with Framingham incidence rates.[20]

The purpose of this report is to present data comparing Anti-Coronary Club experimental and control subjects. Both groups were initially free of clinically identifiable coronary heart disease. These findings indicate that: (1) the experimental group remaining active in the study showed a significant and sustained drop in serum cholesterol levels when compared with the control group, and (2) experimental subjects maintained on the study diet experienced a significantly decreased incidence of coronary heart disease when compared to the control group.

Method

Experimental Group

Since the inception of the Anti-Coronary Club Study in June, 1957, 1,091 males aged 40-59 years have enlisted. The volunteers responded initially to a radio and press call for study participants. Subsequent volunteers were obtained largely from referrals made by original Anti-Coronary Club members. This report considers the 814 subjects of this total who were free of prior evidence of clinical coronary heart disease. The remaining 277 subjects are excluded from this report because of a previous history, or clinical or electrocardiographic evidence of coronary heart disease on entry to the study.

Table 1 shows that as of December 31, 1963, 814 men had accumulated 2,357 person-years of experience while in an *active* status. Active status denotes regular clinic attendance at specified appointment dates for clinical and nutrition review sessions by a panel of physicians, consultation by nutritionists, venipuncture for serum cholesterol determination approximately every five weeks, a yearly medical history and physical examination, and an annual laboratory, electrocardiographic and roentgenographic survey.

Since not all of these men remained in the active state from the time of their enrollment in the study to the present, additional person-years of experience have been accumulated while these individuals lapsed into an *inactive* status. Subjects on inactive status were appraised annually as to health and nutritional status. For about two-thirds of this inactive group this health status appraisal took the form of an annual physical and laboratory examination; in the remainder, communication was attained by phone or in response to a mail questionnaire. The data concerning the men while in this inactive status are presented and discussed later in this report. In no case was the onset of a new coronary disease event involved in the shift of a subject to inactive status.

Control Group

The control group consists of a total of 491 males, aged 40 to 59, who were

Table 1—Experimental and control groups: number of subjects 40-59 years old with no prior coronary history, and person-years of experience

Number and Years	Experimental	Control
Number of subjects admitted		
Total	814	463
40–49	233	235
50–59	581	228
Person-years of experience*		
Total	2,357	1,224
40–49	509	623
50–59	1,848	601

* The indicated person-years of experience represent those accumulated while the subjects were in an *active* status, i.e., while attending the clinic regularly at the specified appointment dates.

recruited as controls since 1959 from among those who had volunteered for examination at the Cancer Detection Clinics of the New York City Department of Health. Of this total, 463 showed no evidence of coronary heart disease according to the same criteria applied to the experimental group. The inducement for enlisting control subjects was the offer of an annual comprehensive cardiovascular examination as an additional routine service. The proposal was made to every male 40-59, of whom about one-third accepted. Those subjects who responded and were assigned to the study as controls can additionally be said to display health consciousness to coronary heart disease as do the volunteers comprising the experimental group. The recruitment process of the control group did not include telling the subjects that they were part of a diet and coronary heart disease study project.

The validity of comparing coronary heart disease incidence in the experimental group consuming the study diet, and the control group remaining on their usual diet, depends on the comparability of other factors associated with coronary heart disease as they exist in the two groups. Thus a detailed demographic and risk factor analysis of the experimental and control groups was performed. As seen in Table 1, there were relatively more 50-59-year-old subjects in the experimental group than in the control. Accordingly, all analyses were performed on an age-specific basis.

In 1960 the experimental and control groups were compared with respect to the demographic characteristics shown in Appendix Table 1. This analysis assured us of a considerable degree of similarity for those characteristics con-

APPENDIX TABLE 1

November, 1960, comparison of demographic characteristics of early experimental and control group members*—percentage distribution

Characteristic	Experimental	Control	Characteristic	Experimental	Control
Number of Subjects	780	93			
Marital Status			Education		
Single	6.5	5.4	Grammar school	12.7	12.0
Married	86.8	89.2	High school	31.8	35.9
Widowed	1.9	2.2	College	49.6	45.7
Divorced and separated	4.6	3.3	Postgraduate	5.9	6.5
			Nativity		
Religion			United States	77.2	70.7
Catholic	9.5	8.7	Germanic countries	4.4	4.9
Protestant	8.2	8.7	Central Europe	6.9	9.8
Jewish	81.1	80.4	USSR and Ukraine	8.4	7.3
Other	1.2	2.2	Other	3.1	7.3
Occupation			Cigarettes Smoked per Day on Entry		
Professional and managerial	50.0	53.3	None	46.4	41.1
Clerical and sales	33.9	28.3	1– 9	7.8	15.4
Service	2.3	2.2	10–29	26.6	26.9
Skilled	12.2	12.0	30–49	15.6	14.1
Semi- and unskilled	1.6	4.4	50–69	3.6	2.6

* Comparison made in November, 1960, when the first 100 subjects had entered the comparison group. However, only 93 of these were in the age group 40–59.

APPENDIX TABLE 2

Comparison of demographic characteristics of total active experimental group and total and matched control group, men 50-59 years old as of December, 1963

Characteristic	Active Experimental	Control	
		Total	Match*
Number of Subjects	478	420†	202
Marital Status			
Single	5.6	6.0	4.7
Married	89.4	89.1	91.2
Widowed	2.9	2.7	1.8
Divorced and separated	2.1	2.2	2.3
Religion			
Catholic	6.8	16.6	6.8
Protestant	8.5	11.4	7.2
Jewish	83.5	69.6	83.8
Other	1.2	2.4	2.3
Occupation			
Professional and managerial	58.9	22.5	59.2
Clerical and sales	26.5	44.1	30.5
Service	1.9	4.9	1.8
Skilled	10.1	19.8	7.6
Semi- and unskilled	2.3	8.7	0.9

Characteristic	Active Experimental	Control	
		Total	Match*
Education			
Grammar school	12.7	14.0	8.7
High school	31.4	48.0	36.5
College	52.7	29.6	40.9
Postgraduate	3.1	8.3	13.9
Nativity			
United States	73.6	67.9	74.3
Germanic countries	3.8	6.5	3.0
Central Europe	6.7	11.8	7.9
USSR and Ukraine	13.2	5.1	7.9
Other	2.7	8.7	6.9
Cigarettes Smoked per Day on Entry			
None	51.9	49.1	51.7
1– 9	9.7	10.8	13.2
10–29	22.4	26.7	25.4
30–49	11.8	12.1	9.3
50–69	4.1	1.3	0.5

* Matched to active experimental group on basis of religion and occupation.
† See footnote **, Table 2.

sidered. However, in October, 1960, in order to enlist more members in the control group, recruitment for volunteer subjects was made through a more personal approach by Anti-Coronary Club staff rather than by the distribution of literature as previously practiced. By the end of 1963, a sufficiently large number of person-years of experience had been accumulated by the control group to warrant a second appraisal of the demographic characteristics of the experimental and control groups.

As is seen in Appendix Table 2, several differences were found. The experimental group now included a greater proportion of subjects in the professional and managerial occupations, a greater proportion of Jewish subjects, and a smaller proportion who had attended college than was found in the control group. Therefore a segment of the control group was randomly selected to match the experimental group on the basis of religion and occupation (Appendix Table 2), variables previously associated with coronary heart disease. Appendix Table 3 compares the number of new events and incidence rates experienced by these matched and unmatched segments of the control group.

In addition to demographic factors of importance associated with a high incidence of coronary heart disease, important risk factors have been identified.[21] In order to compare coronary heart disease incidence rates meaningfully in the experimental and control groups with regard to the effect of the Anti-Coronary Club regimen, analysis of the risk factor status of these two groups upon entry to the study is presented in Table 2. Risk factors under consideration included: (1) hypercholesterolemia, defined as a serum cholesterol level of 260 mg per cent* or more; (2) obesity, as indicated by skin caliper measurements,† a body weight 15 per cent or more over the Metropolitan Life Insurance Company tables of average weight for height, sex, and frame; (3) hypertension, defined as a diastolic blood pressure of 95 mm mercury or more.

A striking characteristic of the experimental group is that only 18.7 per cent of its subjects exhibited none of three risk factors associated with the development of coronary heart disease, on entry compared to 34.3 per cent in the control group. Hypertension was found to be approximately twice as prevalent in the experimental group as in the control. Obesity was frequently encountered in both groups, as 55.6 per cent of the experimental and 46.7 per cent of the control group was found to be at least 15 per cent above optimum weight.

In the 40-49-year-old group, hypercholesterolemia is somewhat more prevalent in the control subjects than in the experimental. However, in the 50-59-year-old group, hypercholesterolemia is slightly greater, and hypertension and obesity are substantially greater in the experimental group compared to the control. Thus in the age group in which coronary heart disease occurs more frequently, the experimental group is weighted toward greater predisposition to coronary heart disease than in the control group with respect to all three risk factors.

It should be stated that both experimental and control groups received similar clinical and laboratory procedures as administered by the professional staff of the Anti-Coronary Club with two exceptions: (1) the detailed dietary evaluation given to the experimental group was not applied to the control since any attention drawn to diet

* The serum cholesterol was determined by the Anderson-Keys modification of the method of Abell-Kendall with a technical error of 2.5 per cent.

† Skin caliper determinations were considered elevated if the total of three measurements was more than 55 mm. The three sites measured were subscapular, brachial and axillary.

APPENDIX TABLE 3

Confirmed new coronary disease events in men 40-59 years old with no prior coronary heart disease on entry for active and inactive study groups and matching* and remainder of active control group

	Number									Incidence Rate per 100,000		
	Total			40–49			50–59					
Group	Subjects	Person-Years	New Events	Subjects	Person-Years	New Events	Subjects	Person-Years	New Events	Total	40–49	50–59
Study												
Active	814	2,357	8	233	509	1	581	1,848	7	339	196	379
Inactive	290	1,482	8	150	720	1	140	762	7	540	139	919
Control, Total	420†	1,224	12	206	623	4	214	601	8	980	642	1,331
Matched	202	639	8	86	292	3	116	347	5	1,252	1,027	1,441
Remainder	218	585	4	120	331	1	98	254	3	684	302	1,181

* Matched to active study group on basis of religion and occupation.
† See footnote **, Table 2.

Table 2—Active* experimental and control groups with no prior coronary heart disease by age by risk factors on entry—number of cases and per cent with indicated risk factor

Risk Factor	Total		40–49		50–59	
	Active Experimental	Control	Active Experimental	Control	Active Experimental	Control
Number of cases	478	420**	67	206	411	214
None of 3 risk factors	18.7	34.3	14.1	35.5	19.5	33.0
Hypercholesterolemia†	39.0	38.1	29.7	36.0	40.5	40.3
Obesity‡	55.6	46.7	71.9	43.9	52.9	49.5
Hypertension§	23.3	11.7	21.9	9.8	23.5	13.5

* Attending clinic regularly at specified appointment dates as of December 31, 1963.
† Serum cholesterol of 260 mg per cent or more.
‡ At least 15 per cent more than optimum weight presented in Metropolitan Life Insurance Company tables of weight for age-height-build-sex, further modified by subjective evaluation of panel of physicians based on skin-caliper measurements and appearance.
§ Diastolic of 95 mm Hg or more.
** Of the 463 who originally entered the control group, 420 were still active as of December 31, 1963.

might induce some change from their usual diet pattern; (2) serum cholesterol levels were determined approximately monthly in the experimental group, and annually in the control. Members of the experimental group have also been followed for about two years longer than those of the control group because the latter was organized in 1959 after it had been demonstrated that a free-living population of experimental study group volunteers could indeed adhere to the study diet.

Diagnostic Criteria

The classification of new events representing myocardial infarction was that used by the Cooperative Study of the American Heart Association.[22] Definite events were identified according to the following list: (1) myocardial infarction, definite; (2) myocardial infarction, definite by ECG alone; (3) coronary thrombosis, definite; (4) coronary sclerosis, definite by autopsy; (5) ECG abnormalities, definite, associated with coronary artery disease; (6) angina pectoris, definite with ECG changes; and (7) angina pectoris, definite, without ECG changes. The criteria for new events were based on those recommended by the New York Heart Association.[23]

The chief cardiologist of the project assigned a classification of "definite event" when in his judgment, criteria for one of the categories were met. He utilized data from the physical examination of subjects, the mail and phone follow-up of inactive subjects, information reported by subjects and their associates, and records from the subjects' families, physicians, hospitalizations, and death certificates. The complete records on all such "definite events" were then submitted to another cardiologist whose sole function on the project was their critical review and evaluation. This cardiologist was not aware whether the record under review was that of an experimental or a control subject; however, submission of a record for his review inferred at least the suspicion of possible pathology. Only confirmed definite events are included in the analyses described later.

The Experimental Diet

A basic nutritional principle of the study diet is to provide approximately equal quantities of the three types of fats: saturated, polyunsaturated and

Table 3—Average serum cholesterol levels of men 40-59 years old with no prior coronary heart disease in active* experimental and control groups by year of participation in study

	Active Experimental		Control	
Year	No.	Cholesterol mg %	No.	Cholesterol mg %
0	478	259.7	463	250.0
1	357	228.2	420	244.5
2	272	231.0	363	242.8
3	184	227.3	249	248.5
4	112	224.6	54	251.6
5	68	225.8		

* Attending clinic regularly at specified appointment dates as of December 31, 1963.

monounsaturated. Beef, mutton, or pork are limited to four meals per week, with the remaining meals comprised of poultry and fish, the latter consumed a minimum of four meals weekly. Butter and hydrogenated shortenings are replaced by high P/S ratio margarines and a minimum of one ounce of vegetable oil daily. Ice cream and hard cheeses are avoided. The diet contains about 30 to 33 per cent of total calories as fat with a ratio of polyunsaturated to saturated fatty acids of 1.25-1.50 to 1.[20] The overweight subjects were placed on a diet averaging 1,600 calories and containing 19 per cent of the total calories as fat.[10] When weight reduction was completed, this diet was changed to the standard study diet by the addition of one ounce of vegetable oil plus additional calories when needed from bread, nuts, fruits, and vegetables.

Results

Serum Cholesterol

Table 3 and Figure 1 show the trends in the level of serum cholesterol of the 40-59-year-old men active in the experimental and control groups.

In the experimental group, a highly significant drop of about 30 mg per 100 ml serum was observed after one year on the study diet, followed by a slight rise in the second year. Thereafter the concentration of serum cholesterol leveled off at about 225 mg per 100 ml. In the control group the serum cholesterol fell about 7 mg per 100 ml after the second year but rose thereafter so that by the end of the fourth year, the latest for which data are available, the average level had returned to its initial concentration.

Although the initial average serum cholesterol level of the control group (250 mg per cent) was significantly lower than that of the experimental group (260 mg per cent), one year of adherence to the study diet by the experimental group served to change the direction of the difference. After one year, the serum cholesterol level of the experimental group (228 mg per cent) was significantly lower than that of the control group (244 mg per cent), despite

Figure 1—Trend of average serum cholesterol of active noncoronary men 40-59 years old in experimental and control groups by year of participation in study

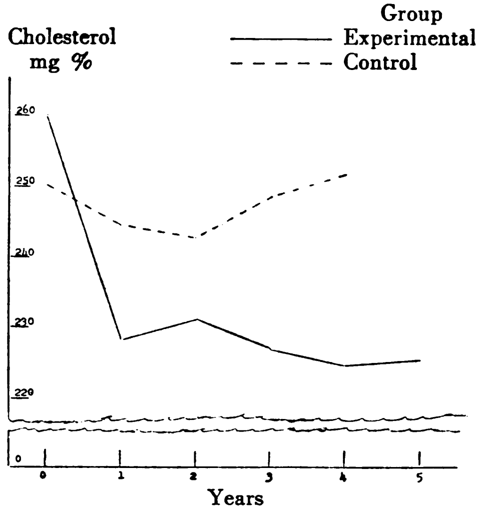


Table 4—Average serum cholesterol level of all men 50-59 years old in active* experimental and control groups at least three years

At End of Year	Cholesterol mg % Experimental	Control
0	261.2	258.1
1	232.4	252.9
2	232.7	247.9
3	229.2	249.4
Number of subjects	113	108

* Attending clinic regularly at specified appointment dates as of December 31, 1963.

the fact that the control group experienced a concurrent decrease. A high order of significance is maintained even after the second year when the smallest difference in serum cholesterol levels was observed.

The significant difference between the benchmark serum cholesterol levels of the experimental and control groups shown in Table 3 is attributable to the fact that there is a greater proportion of younger men in the control group (Table 1). When the factor of age is held constant (Table 4), this difference disappears.

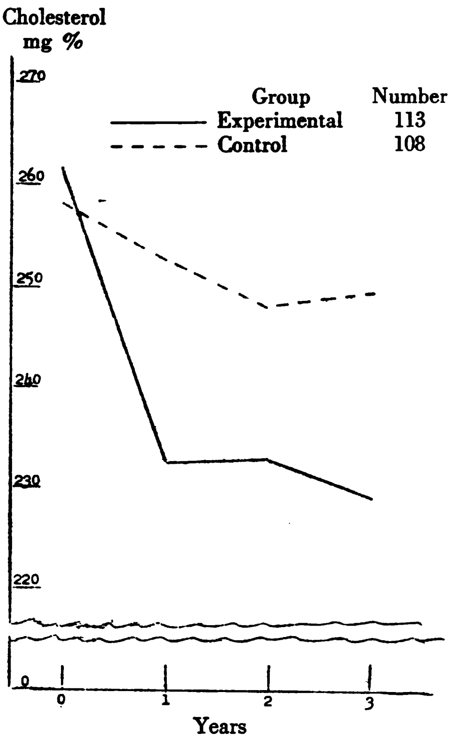
In Table 3 the number of subjects available decreases for the longer periods of observation because of serial admissions to study membership continuing until recently, some losses to follow up in both groups, and shifts from active to inactive status in the experimental group. In order to obviate the possibility that the trend shown in Figure 1 is an artifact because of the decreasing numbers of subjects, the serum cholesterol levels of a constant cohort in each group were analyzed. The cohorts comprised all men 50-59 years of age in the experimental and control group in the study for three years or more.

The trends for the 113 men in the experimental cohort and the 108 men in the control cohort as seen in Table 4 and Figure 2 confirm those of the total active experimental and control groups presented in Table 3 and Figure 1.

New Coronary Events and Incidence Rates

Table 5 presents data accrued by the experimental and control groups in terms of accumulated person-years of experience, number of confirmed new coronary events, and incidence rates per 100,000. In the course of the life of the study during which 2,357 person-years of experience were accumulated in the active state, eight confirmed new coronary events occurred to yield an over-all incidence rate of 339 per 100,000. This is comprised of age-

Figure 2—Trend of average serum cholesterol level of cohorts of active noncoronary men 50-59 years old in study at least three years



specific rates of 196 and 379 per 100,000 for the 40-49 and 50-59-year-old men, respectively.

Similarly, the 463 men of the control group in comparable age categories have accumulated 1,224 person-years of experience and 12 confirmed new coronary events, resulting in a morbidity rate of 980 per 100,000. Once again, this may be separated into 642 and 1,331 per 100,000 for the 40-49 and 50-59-year-old men, respectively.

In addition to the experience of the *active* study members, Table 5 also considers the men who were formerly active but are now in the *inactive* status. In this category 290 men have accumulated 1,482 person-years of experience after shifting from active participation in the experimental group. While in the inactive status, eight confirmed new coronary events have occurred yielding an incidence rate of 540 per 100,000 with a rate of 139 per 100,000 for the men 40-49 years old and 919 per 100,000 for men 50-59 years old.

The rate of development of new coronary heart disease in the Anti-Coronary Club by age in both the experimental and control groups is shown in Table 6, together with similar rates experienced by other groups which have been under observation without changing their diet.

Of the eight new coronary disease events for experimental subjects on active status, seven occurred during the 1,353 person-years of experience accumulated during the first two years of each individual's participation in the study (Table 7). Only one of these eight new events occurred during the 1,004 person-years of active experience accumulated subsequent to the first two years of participation of each individual, when presumably the diet had a fuller opportunity to exert its physiological effect.

Table 5—New coronary disease events* and incidence rates per 100,000 person-years in study and control subjects free of coronary heart disease, 40-59 years old

		Experimental		
		Active†	Inactive‡	Control
Number of subjects	Total	814	290	463
	40–49	233	150	235
	50–59	581	140	228
Years of experience	Total	2,357	1,482	1,224
	40–49	509	720	623
	50–59	1,848	762	601
Confirmed new events*	Total	8	8	12
	40–49	1	1	4
	50–59	7	7	8
Incidence rates per 100,000 person-years of experience	Total	339	540	980
	40–49	196	139	642
	50–59	379	919	1,331

* As determined by the criteria of the New York Heart Association based on clinical, historical, and electrocardiographic evidence.

† Experience accumulated while subject was in the status of regularly attending the clinic at specified appointment dates.

‡ Experience accumulated while attending clinic annually or with successful regular contact by mail or phone since active attendance at panel or nutritionist sessions were discontinued. No professional supervision of diet in this phase.

Table 6—Incidence rates per 100,000 years of experience of new coronary heart disease in other study groups under observation

Group	Incidence Rate per 100,000 Person-Years Males Aged	
	40–49	50–59
ACC active experimental	196	379
ACC control	642	1,331
Framingham*	647	1,855
Albany†	694	1,870‡

* Kannel, Dawber, et al. Ann. Int. Med. 55:33, 1961.
† Doyle, et al. A.J.P.H. 47:25, 1957 (Suppl.).
‡ Data published only for age group 50-54. Total 50-59 group estimated by weighting on basis of Framingham distribution of rates:

Age	Framingham	Albany
50–54	1,275	1,290
50–59	1,855	

Similarity of 40-49 and 50-54-year-old ratio provides validity for this procedure.

Comparison of the rate of development of new coronary disease in the control and experimental groups during these first two years of their experience, indicates no statistically significant difference between the two groups. However, the rate in the experimental group for the period subsequent to the first two years of participation of each individual was significantly lower than for the same group during the first two years of participation ($p<0.01$). Furthermore, the rate in the experimental group subsequent to the first two years of participation was significantly lower than in the control group for the comparable period of observation ($p<0.01$).

Of the 814 entrants to the experimental group, 46 or 5 per cent of the total dropped out of the study. Dropout status signifies discontinuation of all contact with the study after a period of active status (averaging 15 months). These 46 dropouts were traced by mail questionnaire, phone interviews, and home visits in regard to subsequent health status. This follow-up investigation was made to determine whether the frequency of new coronary events that may have occurred in this group of dropouts could affect the interpretation of the major findings in our active and inactive experimental subjects. This analysis revealed that a death from coronary heart disease had occurred in a subject four years after he had dropped out of the study with less than a year's participation. A nonfatal new event also occurred four years after another subject had dropped out following four months' participation in the study. Of the remaining 44 dropouts, 42 were known to be alive and reportedly free of new coronary events; only two remain with unknown follow-up status.

A calculation was made of the observed and expected new coronary events in the total experimental group, which utilized the two reported new events obtained by following the dropouts and which also was based on the unlikely assumption that the two cases remaining with unknown status after follow-up had actually experienced new coronary events. This calculation confirms the

Table 7—New coronary events and person-years of experience in men 40-59 years old with no prior coronary history by group by year of follow-up

During Year	Person-Years of Experience: Active Experimental	Person-Years of Experience: Control	New Events: Active Experimental	New Events: Control
1	760	460	4	3
2	593	392	3	3
3	430	277	0	3
4	300	95	0	3
5	198	—(a)	1	–(a)
6	76	—(a)	0	–(a)

(a) Control group activated two years after experimental group.

highly significant differences already noted between the observed number of new events and the expected numbers, and in no way alters our interpretation of these findings.

Among the 463 individuals in the control group, 43 subjects dropped out of the study after their initial visit. The control dropouts were followed using the same procedures applied to the experimental group dropouts. Among the 43 dropouts, information was available on 28 subjects and no new events were reported. Although follow-up data in our controls are not as complete as in the experimental group, any additional new coronary events which may have occurred among control dropouts remaining with status unknown could only have accentuated the difference already observed in coronary heart disease incidence between the experimental and control groups.

Out of the 814 experimental group subjects, there have been 18 known deaths from causes other than coronary heart disease among individuals who had not experienced a new coronary event. This is in comparison to six such deaths out of the 463 individuals in the control group. All but two of these 24 deaths were in the 50-59 age group. The rates for these deaths in the 50-59 age group were 689 per 100,000 person-years in the experimental group, and 666 per 100,000 in the control group. The difference between these two rates is very slight and not statistically significant.

Discussion

The data presented indicate that the incidence of new coronary events among initially coronary-free full participants in the Anti-Coronary Club's program was significantly lower than that among its control group, and also lower than incidence rates reported in studies[24,25] of comparable age groups. It seems reasonable to attribute this difference primarily to the effects of the Anti-Coronary Club's program, the major feature of which was supervised adherence to the Study Diet. The following reasons are cited to substantiate this conviction:

1. The group of entrants into the experimental group had no initial predilection for reduced coronary heart disease incidence in comparison with the control group, as judged by the frequency of the three physiologic risk factors that have been found to be significant predictors of subsequent heart disease in the Albany and Framingham studies.[24,25] If anything, the Anti-Coronary Club's experimental group was somewhat more prone to the development of coronary disease, since it had a lower proportion free of these three risk factors than did the control group. These data are particularly important in connection with the fact that these groups both consisted of volunteers. Without this evidence, one could not have dismissed the hypothetical possibility that the volunteers for the experimental program differed from the voluntary controls in a way that would be expected to result in a lower rate of new coronary disease in the experimental group, even if the experimental program had no effect.

As already indicated, there was a tendency for the experimental group subjects to shift to inactive status if they were obese younger adults who found adherence to the prescribed diet difficult, or if they could not obtain sufficient time off from their jobs to maintain the frequent schedule of visits to the Anti-Coronary Club's facilities. Despite these selective factors involved in shifting to inactive status, those remaining active apparently were not initially biased with respect to risk factors related to a low rate of coronary disease incidence in comparison with the control group.

2. Those remaining in the active ex-

perimental group appear to have generally maintained adherence to the study diet, as judged by regular and frequent interviews with the Anti-Coronary Club nutritionists, and by the progressive increase in the linoleic acid component of their depot fat.

3. A substantial and statistically significant decrease in serum cholesterol levels occurred during the first year of active status in the experimental group, in comparison with the Anti-Coronary Club control group. The serum cholesterol level in the active experimental group remained essentially stabilized at this lower level throughout the next several years of follow-up. Numerous studies have shown an association between high serum cholesterol levels and high incidence rates of coronary heart disease in various population groups.[1] The Albany and Framingham studies[24,25] have shown that hypercholesterolemia is a significant predictive risk factor for subsequent coronary disease. In metabolic ward studies,[15-17] carefully controlled diets similar in composition to the Anti-Coronary Club Study Diet have also lowered the serum cholesterol levels in human subjects.

4. There was a substantial and statistically significant decrease in the incidence rate of new coronary disease in the active experimental group between the first two years of participation in the study and the period from the third through the fifth years despite the increasing age of the group. In contrast, the rate increased with the passage of time in the Anti-Coronary Club's control group, as would be expected. These data are consistent with an effect of the program in preventing the development of new coronary heart disease. They argue against the interpretation of the over-all significantly low incidence rate in the experimental group being due to any unknown initial bias in that group, such as any unusual characteristic of the volunteers or any unequal exclusion of cases with prior coronary disease from the experimental and comparison groups. Such biases would be expected to either exert a constant effect as the follow-up period increased, or to have their strongest influence at the beginning of the study with the difference in incidence rates between experimental and control groups narrowing as time progressed.

5. As mentioned previously, a substantially higher proportion of professional and managerial occupations and subjects of the Jewish religion were found among experimental group subjects remaining on active status than in the control group. Thus, it was decided to adjust analytically for differences in occupation and religion. The maximum possible number of subjects with no prior coronary disease history were selected from the total Anti-Coronary Club's control group to match the distribution of occupation and religion found in the experimental group. The selection from each category of the control group for cases to be included in the matching sample was performed using strict random sampling methods, without regard for subsequent new coronary heart disease events. It was found that in each age group (Appendix Table 3) the incidence rate of new coronary disease events in the matching control sample exceeded the rate in the total unmatched control sample. The difference between the rates in the active experimental group and the matched control group are thus greater than between the active experimental group and the original total control group. Therefore, the original statistically significant differences in the rates between the active experimental group and the total control group are not due to the occupational differences between these groups. This analysis complements the one previously discussed showing no coronary risk factor bias toward low heart disease incidence in the active experimental group in comparison with the total Anti-Coronary Club control group.

6. The incidence rates in the Anti-Coronary Club control group are not high in comparison to those in other prominent prospective studies. The significantly lower incidence rate in the Anti-Coronary Club's experimental group than in its control group is therefore not due to an unusually high rate in the latter group.

Final answers to many important questions relevant to the effects of the Anti-Coronary Club program have not yet been obtained. The number of new coronary events through the end of the observation period for this report is admittedly small. However, the follow-up of the experimental and control groups will continue and, as additional data accumulate, more meaningful analyses will be possible on a number of questions. Among these are whether the relatively low incidence rate remains so in the experimental group as participation continues, whether there is a difference in case-fatality among the new cases of coronary disease in the experimental and control groups, and whether the new coronary events which occur among the long-term full participants in the experimental program can be related to other characteristics.

Public Health Implications

Two decades of international epidemiological investigations of diet and coronary heart disease, and the data emanating from the cardiovascular studies at Framingham and Albany, have identified the elevated serum cholesterol level as a prime factor of risk in the development of coronary heart disease. The statistical relationship between the level of serum cholesterol and the degree of risk in developing coronary heart disease has been emphasized by Cornfield,[26] who indicated that each 1 per cent difference in the average serum cholesterol level of population groups is associated with a 2.66 per cent difference in coronary heart disease risk at all levels of serum cholesterol.

The present data from the Anti-Coronary Club have shown that the level of serum cholesterol can be effectively lowered over the course of a five-year period without incurring a rebound. Moreover, such effective and prolonged lowering of serum cholesterol is associated with an incidence of coronary heart disease in subjects on the study diet which is significantly lower compared to our control group and to other populations under long-term observation consuming the usual American diet.

The public health significance of our salutary effect on coronary heart disease morbidity comes into proper perspective when it is realized that 30 to 40 per cent of all American males 40 to 59 years of age exhibit serum cholesterol levels above 260 mg per cent and are therefore exposed to six times the risk of developing coronary heart disease compared to populations whose serum cholesterol is 220 mg per cent or less.[24,27]

It becomes difficult to escape the conviction that the high levels of serum cholesterol observed in males age 40 to 59 warrant prevention by avoidance of the rapid increase in serum cholesterol to levels above 220 mg per cent observed in young adult males age 27 and over.[27] However, the use of serum cholesterol-lowering diets in infancy and childhood would not appear indicated at the present time until further knowledge is acquired concerning the particular fatty acid requirements of infants, especially in regard to vitamin E nutriture. While the rise in serum cholesterol with increasing age is more gradual in females, there is no reason why women should wait for the menopause to institute dietary control of serum cholesterol.

Over the course of the past five decades there has been an increase in the consumption of beef and dairy products and an increase in the daily caloric contribution by fat from approximately 30-33 per cent to 40-44 per cent of total calories. Two-thirds of this fat consumption is saturated. Though not the sole cause, this trend has almost certainly played a major role in causing what may be called "national dietary hypercholesterolemia."

High levels of serum cholesterol, associated as they are with increased risk of developing coronary heart disease,[24] can hardly be considered "normal" or "desirable." It is therefore logical to assume that a diet responsible, even in part, for a risk factor which predisposes to a disease as serious and as prevalent as coronary heart disease cannot be considered optimally physiologic. A critical reappraisal of our nutritional way of life would therefore appear indicated. We realize that a consideration of changes in our national diet pattern requires profound study and involves great responsibility. While we have investigated certain effects of the study diet on serum vitamin levels and depot fat composition, not all the possible long-term metabolic effects of our study diet are now known. Confirmation of the presently described results would also be desirable. However, while the gratifying gains in public health nutrition afforded by advances in the nutrition sciences and incorporated in the American diet must not be nullified, the virtues of our present diet patterns should not be extolled so vociferously that they are not considered susceptible to improvement.

We are, in fact, faced with the strong possibility that a diet pattern based on the principle of moderation in saturated fat consumption and which provides a varied, nutritionally sound diet while lowering serum cholesterol, may constitute a contribution to the development of a more physiologically optimal diet pattern for adults. The constituents of this diet are available from food markets everywhere, are palatable, fulfill the nutrient requirements of the National Research Council and are free of food fad characteristics. We emphasize, however, that a change in the diet pattern correcting the current overconsumption of saturated fats should not be misconstrued to mean a pattern in which polyunsaturated fats predominate, or in which any other food group is overemphasized to the exclusion of other foods supplying essential nutrients. It should also be emphasized that the apparently successful experience reported here involved a continuing program of supervised diet adherence and periodic medical examination. It is not yet known whether similar benefits can be derived from less comprehensive programs or whether any hazards may be inherent in attempts to oversimplify the diet pattern or use short-cut programs or educational efforts.

If a consensus of medical and public health judgment concurs that dietary changes for the public are indicated, how are these to be implemented? Public health officials bear the responsibility of designing and operating nutrition education programs. The practicing physician must be made aware of, and must familiarize himself with the meaning of the serum cholesterol level, the principles of the diet which can control it, and the difficulties likely to be encountered by his patient.[11] Industry has already shown that palatable fat-modified foods can be produced; such foods can effectively lower serum cholesterol under experimental conditions.[28] It would be up to government to develop suitable standards and labeling regulations enabling easier consumer identification of foods useful in a serum cholesterol-lowering regimen. It would also no longer appear prudent for governmental agencies to urge the public to increase consumption of products containing large quantities of saturated fat on the grounds that such products exist in surplus.

Many factors operate in the causation of coronary heart disease; however, the comprehensive experience of the Anti-Coronary Club in lowering serum cholesterol and coronary heart disease incidence appears to have established a reasonable basis for public health action. Though the problems of program planning and implementation will be many and complex, there now appears to be real hope that effective programs for the control of coronary heart disease can eventually be developed.

Summary

1. The Anti-Coronary Club Study Project represents an epidemiological approach to test the hypothesis that adherence to a serum cholesterol-lowering diet will be associated with a decreased incidence of coronary heart disease. This diet consists of a partial replacement of foods predominating in saturated fats by those rich in polyunsaturated fatty acids. Eight hundred and fourteen volunteer males free of coronary heart disease, age 40-59 years were instructed and supervised in its use for periods up to seven years accumulating a total of 2,357 person-years of experience. The control group was comprised of 463 males of the same age group who remained on their usual diet pattern, were free of coronary heart disease and were followed for a five-year period accumulating a total of 1,224 person-years of experience. The control subjects were enlisted from men attending the City of New York Department of Health Cancer Detection Clinics.

2. Adherence to the study diet effectively lowered the serum cholesterol within the first year and maintained the lowered levels up to six years, the end of the observation period. After one year on the study diet, the average level of serum cholesterol in the experimental group had fallen from 260 mg per cent to 228 mg per cent and remained at approximately that level for the following four years. In the control group, the average initial level was 250 mg per cent and after a drop of 7 mg per cent at two years, it returned to the initial level at the end of four years.

3. Comparisons of the proportions of the experimental and control groups exhibiting the Framingham-elucidated risk factors associated with coronary heart disease (obesity, hypertension, hypercholesterolemia) indicate that from this aspect, the experimental groups showed no inherent propensity to experience lower incidence rates. On the contrary, a significantly greater proportion of the controls entered the study free of these risk factors, and thus there was no bias in favor of a lower incidence rate in the experimental group.

4. A significantly lower incidence of coronary heart disease was observed in the experimental group consuming the study diet compared to the control group who received no dietary instruction or supervision. In men 40-49 years old, there was one new coronary event in the active experimental group and four in the control group, yielding incidence rates of 196 per 100,000 person-years and 642 per 100,000 person-years, respectively. In the 50-59 year group, there were seven new coronary events in the active experimental group and eight in the control group yielding rates of 379 and 1,331, respectively. The experience of the experimental and control groups indicates that, in the context of the study setting, a period of one to two years is necessary before the study program exerts its full effect. In the first two years of follow-up, coronary heart disease incidence rates of the two groups are not significantly different. After the first two-year period, the incidence rate in the active experimental group was substantially and significantly lower than that during the first two years and was also significantly lower than the rate in

the control group for the comparable period of observation.

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This manuscript is dedicated to the memory of Dr. Norman Jolliffe, whose work the authors are privileged to continue.

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Drs. Christakis, Rinzler, Winslow, Jampel, Stephenson, Friedman, Fein, and Mr. Archer are associated with the Bureau of Nutrition, City of New York Department of Health. Dr. Kraus is associate director, Office of Research, City of New York Department of Health; and Dr. James, former commissioner of health, City of New York Department of Health, is presently dean, Mount Sinai School of Medicine, New York City.

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